Please amend the claims as follows:

Cancel claim 23, without prejudice.

Amend claims 1, 2, 4, 7-17 and 21 to read as follows:

1. (Four times amended) A method for sequencing nucleic acid molecules, comprising the steps of:

a) providing at a first location a first plurality of single stranded nucleic acid molecules that have the same sequence as one another and that are hybridized to primers in a manner to allow template-directed primer extension when in the presence of nucleotides and a nucleic acid polymerase;

b) providing at a second location, which is different from the first location, a second plurality of single stranded nucleic acid molecules that have the same sequence as one another, but that have different sequence from the sequence of the single stranded nucleic acid molecules at the first location, and that are also hybridized to primers in a manner to allow template-directed primer extension when in the presence of nucleotides and a nucleic acid polymerase;

c) providing each said first and second location with a nucleic acid polymerase and a given nucleotide in labeled and unlabeled form under conditions that allow template-directed extension of the primers;

d) detecting whether or not said labelled nucleotide has been used for primer extension at each said first and second location by determining whether or not the label present on said nucleotide has been incorporated into extended primers, and if said labelled nucleotide has been used in primer extension this step further comprises detecting how many of said nucleotides have been used per extended primer; and

e) repeating steps c) and d) at least 19 times without removing incorporated labels so that extended primers each comprising a plurality of labels are provided;

whereby the sequences of the nucleic acid molecules at the first and second locations are obtained by reference to the number and type of nucleotides used in primer extension at said first and second locations.

E2

2. (Twice Amended) A method according to claim 1, further comprising determining the complementary sequences of all or part of the sequences obtained in step e).

E3

4. (Twice Amended) A method according to claim 1, further comprising after step c) removing excess nucleotides that have not been used in primer extension.

7. (Twice amended) A method for sequencing nucleic acid molecules, comprising the steps of:

E4

a) providing at each of a plurality of locations a plurality of single stranded nucleic acid molecules that have the same sequence as one another but have different sequences from the sequence of the single stranded nucleic acid molecules at any other location among said plurality of locations, wherein said single stranded nucleic acid molecules are hybridized to primers in a manner to allow template-directed primer extension when in the presence of nucleotides and a nucleic acid polymerase;

b) providing each of said plurality of locations with a nucleic acid polymerase and a given nucleotide in labeled and unlabeled form under conditions that allow template-directed extension of the primers, wherein the ratio of said labeled and unlabeled form is chosen such that labeled nucleotides are used in primer extension less than 50% of the time;

c) detecting whether or not said labelled nucleotide has been used for primer extension at each of said plurality of locations by determining whether or not the label present on said nucleotide has been incorporated into extended primers and if said labelled nucleotide has been used in primer extension this step further comprises detecting how many of said nucleotides have been used per extended primer; and

d) repeating steps b) and c) one or more times so that extended primers each comprising a plurality of labels are provided;

wherein the sequence of the nucleic acid molecules at each of said plurality of locations is obtained by reference to the number and type of nucleotides used in primer extension at each

of said plurality of additional locations, and wherein said plurality of locations consists of 10 or more locations such that 10 or more nucleic acid molecules having different sequences are fully or partially sequenced at 10 or more different locations simultaneously.

8. (Three Times Amended) A method according to claim 7, wherein said plurality of locations consists of 100 or more locations such that 100 or more nucleic acid molecules having different sequences are fully or partially sequenced at 100 or more different locations simultaneously.

E4 cont.

9. (Three Times Amended) A method according to claim 8, wherein said plurality of locations consists of 1000 or more locations such that 1000 or more nucleic acid molecules having different sequences are fully or partially sequenced at 1000 or more different locations simultaneously.

10. (Twice Amended) A method according to claim 1, wherein each of four different nucleotides is provided in separate primer extensions.

E5

11. (Amended) A method according to claim 10, wherein said four different nucleotides are provided in a predetermined order in repeated cycles.

12. (Twice Amended) A method according to claim 10, wherein the four different nucleotides are (i) dATP, (ii) dTTP or dUTP, (iii) dGTP and (iv) dCTP in labelled and unlabeled forms.

13. (Amended) A method according to claim 10, wherein the four different nucleotides are ATP, UTP, GTP and GTP in labelled and unlabeled forms.

E6

14. (Twice Amended) A method according to claim 1, wherein step d) is carried out without removing the nucleic acid molecules from the first and second locations.

15. (Three Times Amended) A method for sequencing nucleic acid molecules, comprising the steps of:

a) providing at a first location a first plurality of double stranded nucleic acid molecules that have the same sequence as one another and that have nicks therein in a manner to allow nick translation when in the presence of nucleotides and a nucleic acid polymerase;

b) providing at a second location, which is different from the first location, a second plurality of double stranded nucleic acid molecules that have the same sequence as one another, but that have a different sequence from the sequence of the single stranded nucleic acid molecules at the first location, and that have nicks therein in a manner to allow nick translation when in the presence of nucleotides and a nucleic acid polymerase;

E7

c) providing each said first and second location with a nucleic acid polymerase and a given nucleotide in labeled and unlabeled form under conditions that allow nick translation, wherein the ratio of said labeled and unlabeled form is chosen such that labeled nucleotides are used in nick translation less than 50% of the time;

d) detecting whether or not said labelled nucleotide has been used for nick translation at each said first and second location by determining whether or not the label present on said nucleotide has been incorporated into said double stranded nucleic acid molecules, and if said labeled nucleotide has been used in nick translation this step further comprises detecting how many of said nucleotides have been used per translated nick; and

e) repeating steps c) and d) one or more times so that nick translation products each comprising a plurality of labels are provided;

whereby the sequences of the nucleic acid molecules at the first and second locations are obtained by reference to the number and type of nucleotides used in nick translation at each of said first and second locations.

16. (Twice Amended) A method for sequencing nucleic acid molecules, comprising the steps of:

a) providing at a first location a single stranded nucleic acid molecule that is hybridized to a primer in a manner to allow template-directed primer extension when in the presence of nucleotides and a nucleic acid polymerase;

b) providing at a second location, which is different from the first location, a single stranded nucleic acid molecule that has a different sequence from the sequence of the single stranded nucleic acid molecule at the first location, and that is also hybridized to a primer in a manner to allow template-directed primer extension when in the presence of nucleotides and a nucleic acid polymerase;

E8

c) providing each said first and second location with a nucleic acid polymerase and a given labelled nucleotide under conditions that allow template-directed extension of the primers;

d) detecting whether or not said labelled nucleotide has been used for primer extension at each said first and second location by determining whether or not the label present on said nucleotide has been incorporated into extended primers, and if said labelled nucleotide has been used in primer extension this step further comprises detecting how many of said nucleotides have been used per extended primer; and

e) repeating steps c) and d) one or more times so that extended primers each comprising a plurality of labels are provided and the sequences of the nucleic acid molecules at the first and second locations are obtained by reference to the number and type of nucleotides used in primer extension at said first and second locations;

f) removing said extended primers at said first and second locations;

g) hybridizing the single standed nucleic acid molecules at said first and second locations to a second primer such that said single nucleic acid molecules can serve as templates for extension of the 3' end of the primers;

h) providing each said first and second location with a polymerase and one or more types of label-free nucleotide under conditions allowing template-directed extension of the primer to produce a primer extension product;

i) providing each said first and second location with a nucleic acid polymerase and a given labelled nucleotide under conditions that allow template-directed extension of said primer extension product;

E8 cont.

j) detecting whether or not said labelled nucleotide has been used for extension of said primer extension product at each said first and second location by determining whether or not the label present on said nucleotide has been incorporated into said primer extension product, and if said labelled nucleotide has been used in extension of said primer extension product this step further comprises detecting how many of said nucleotides have been used; and

k) repeating steps i) and j) one or more times so that extended primers each comprising a plurality of labels are provided and the sequences of the nucleic acid molecules at the first and second locations are obtained by reference to the number and type of nucleotides used in primer extension at said first and second locations.

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17. (Four Times Amended) A method for sequencing nucleic acid molecules, comprising the steps of:

E9

a) providing at a first location a first plurality of single stranded nucleic acid molecules that have the same sequences as one another and that are hybridized to primers in a manner to allow template-directed primer extension when in the presence of nucleotides and a nucleic acid polymerase;

b) providing at a second location, which is different from the first location, a second plurality of single stranded nucleic acid molecules that have the same sequences as one another, but that have different sequences from the sequences of the single stranded nucleic acid molecules at the first location, and that are also hybridized to primers in a manner to allow template-directed primer extension when in the presence of nucleotides and a nucleic acid polymerase;

c) providing each said first and second location with a nucleic acid polymerase and a given nucleotide in labelled and unlabelled form under conditions that allow template-directed extension of the primers, wherein the ratio of said labeled and unlabeled form is chosen such that labeled nucleotides are used in primer extension less than 50% of the time;

E9 cont.

d) detecting whether or not said labelled nucleotide has been used for primer extension at each location by determining whether or not the label present on said nucleotide has been incorporated into extended primers, and if said labelled nucleotide has been used in primer extension, this step further comprises detecting how many of said nucleotides have been used per extended primer;

e) repeating steps c) and d) one or more times so that extended primers each comprising a plurality of labels are provided;

whereby the sequences of the nucleic acid molecules at the first and second locations are obtained by reference to the number and type of nucleotides used in primer extension at said first and second locations.

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21. (Four Times Amended) A method of sequencing a target nucleic acid comprising:

E10

(a) hybridizing the target nucleic acid to a primer to produce a hybridized target nucleic acid/primer whereby the target nucleic acid can serve as a template for extension of the 3' end of the primer,

(b) incubating the hybridized target nucleic acid/primer with a polymerase and a type of nucleotide bearing a label under conditions allowing template-directed extension of the primer if the nucleotide type can be incorporated as the complement of a corresponding nucleotide of the target;

c) measuring first label incorporated into the primer to determine whether, and if so, by how many base increments, the primer has been extended by incorporation of the nucleotide type;

(d) incubating the hybridized primer/target nucleic acid with a polymerase and a different type of nucleotide bearing a label under conditions allowing template-directed extension of the primer if the different nucleotide type can be incorporated so as to be complementary to a corresponding nucleotide in the target:

(e) measuring incremental label incorporated into the primer due to the previous incubating step to determine whether, and if so, by how many base increments, the primer has been extended by incorporation of the different nucleotide type;

(f) repeating steps (b) - (e) so that extended primer comprising a plurality of labels is provided, until a desired portion of the target sequence can be determined from the incremental base incorporations into the primer;

(g) removing said extended primer;

E1D cont.

(h) hybridizing the target nucleic acid to a second primer to produce a second hybridized target nucleic acid/primer such that the target nucleic acid can serve as a template for extension of the 3' end of the primer;

(i) incubating said second hybridized target nucleic acid/primer with a polymerase and one or more types of label-free nucleotide under conditions allowing template-directed extension of the primer to produce a second primer extension product;

(j) incubating said second primer extension product with a polymerase and a type of nucleotide bearing a label under conditions allowing template-directed primer extension;

(k) measuring the label incorporated into said second primer extension product to determine whether, and if so, by how many base increments, said second primer extension product has been extended by incorporation of the nucleotide type;

(l) incubating said second primer extension product with a polymerase and a type of nucleotide bearing a label different from the label of step (j) under conditions allowing template-directed extension of the primer;

(m) measuring incremental label incorporated into said second primer extension product in step (l) to determine whether, and if so, by how many base

E10 cont.

increments, said second primer extension product has been extended by incorporation of the nucleotide type of step (l); and

(n) repeating steps (j) - (m) so that extended second primer comprising a plurality of labels is provided, until a desired portion of the target sequence can be determined from the incremental base incorporations into the second primer.

Add new claims as follows:

25. (New) A method according to claim 9, wherein said plurality of locations consists of 1,000,000 or more locations such that 1,000,000 or more nucleic acid molecules having different sequences are fully or partially sequenced at 1,000,000 or more different locations simultaneously.

26. (New) A method according to claim 17, wherein each of four different nucleotides in labeled and unlabeled form is provided in separate primer extensions.

E11

27. (New) A method according to claim 26, wherein said four different nucleotides are provided in a predetermined order in repeated cycles.

28. (New) A method according to claim 26, wherein said four different nucleotides are (i) dATP, (ii) dTTP or dUTP, (iii) dGTP and (iv) dCTP.

29. (New) A method according to any one of claims 7-9, 15, 17 and 25, wherein the ratio of said labeled and unlabeled form is chosen such that labeled nucleotides are used in primer extension less than 20% of the time.

30. (New) A method according to claim 29, wherein the ratio of said labeled and unlabeled form is chosen such that labeled nucleotides are used in primer extension less than 10% of the time.

31. (New) A method according to claim 1 or 17, wherein each said first and second location has an area of a size in the range of from 100 nm to 2 cm when measured across the largest dimension.

32. (New) A method according to claim 31, wherein each said first and second location has an area of a size in the range of from 500 nm to 5 mm when measured across the largest dimension.

33. (New) A method according to claim 7, 8, 9 or 25, wherein each said location has an area of a size in the range of from 100 nm to 2 cm when measured across the largest dimension.

E11 cont.

34. (New) A method according to claim 33, wherein each said location has an area of a size in the range of from 500 nm to 5 mm when measured across the largest dimension.

35. (New) A method according to claim 1 or 17, said method further comprising before steps a) and b) a step of adding to said single stranded nucleic acid molecules a nucleotide sequence which hybridizes to said primers.

36. (New) A method according to claim 7, 8, 9 or 25, said method further comprising before step a) a step of adding to said single stranded nucleic acid molecules a nucleotide sequence which hybridizes to said primers.

37. (New) A method according to claim 1, further comprising before said step c) a step of providing at a third location, which is different from said first and second locations, a plurality of single stranded nucleic acid molecules that have the same sequences as one another, and have the same sequence as the single stranded nucleic acid molecules at said first location, and that are also hybridized to primers in a manner to allow template-directed primer extension when in the presence of nucleotides and a nucleic acid polymerase, and said method further comprising the steps of

f) providing said third location with a nucleic acid polymerase and a given nucleotide in labeled and unlabeled form under conditions that allow template-directed extension of the primers;

g) detecting whether or not said labeled nucleotide has been used for primer extension at said third location by determining whether or not the label present on said nucleotide has been incorporated into extended primers, and if said labeled nucleotide has been used in primer extension this step further comprises detecting how many of said nucleotides have been used per extended primer; and

E11 cont.

h) repeating steps f) and g) at least 19 times without removing incorporated labels so that extended primers each comprising a plurality of labels are provided;

whereby the sequence of the nucleic acid molecules at said third location is obtained by reference to the number and type of nucleotides used in primer extension at said third location.

38. (New) A method according to claim 17, further comprising before said step c) a step of providing at a third location, which is different from said first and second locations, a plurality of single stranded nucleic acid molecules that have the same sequences as one another, and have the same sequence as the single stranded nucleic acid molecules at said first location, and that are also hybridized to primers in a manner to allow template-directed primer extension when in the presence of nucleotides and a nucleic acid polymerase, and said method further comprising the steps of

f) providing said third location with a nucleic acid polymerase and a given nucleotide in labeled and unlabeled form under conditions that allow template-directed extension of the primers, wherein the ratio of said labeled and unlabeled form is chosen such that less than 50% of primer extensions use labeled nucleotides;

g) detecting whether or not said labelled nucleotide has been used for primer extension at said third location by determining whether or not the label present on said nucleotide has been incorporated into extended primers, and if said

labeled nucleotide has been used in primer extension, this step further comprises detecting how many of said nucleotides have been used per extended primer;

h) repeating steps f) and g) one or more times so that extended primers each comprising a plurality of labels are provided;

whereby the sequence of the nucleic acid molecules at the third location is obtained by reference to the number and type of nucleotides used in primer extension at said third location.

E11 cont.

39. (New) A method according to claim 1 or 17, wherein said first and second locations are provided on a solid support.

40. (New) A method according to claim 39, wherein said solid support is a planar solid support.

41. (New) A method according to claim 40, wherein said planar solid support is a glass support.

42. (New) A method according to claim 1 or 17, wherein said first and second locations are provided on a semi-solid support.

43. (New) A method according to claim 42, wherein said semi-solid support is a gel.

44. (New) A method according to claim 7, 8, 9 or 25, wherein said plurality of locations are provided on a solid support.

45. (New) A method according to claim 44, wherein said solid support is a planar solid support.

46. (New) A method according to claim 45, wherein said planar solid support is a glass support.